

## **Amendments to the Claims**

This listing of claims will replace all prior versions and listings of claims in the above-identified application:

### **Listing of Claims**

**Claim 1** (Currently Amended): A method of determining and outputting a probe candidate that is utilized for designing a base sequence to be used as a probe which is hybridized with a nucleic acid fragment to perform analysis, comprising:

a generation step of generating a tree in which a plurality of partial base sequences obtained on the basis of a plurality of target base sequences are arranged on nodes, said target base sequences including a base sequence to be examined;

an extraction step of extracting a partial base sequence indicated by nodes present on a path from one of the nodes to a root node on the tree, the partial base sequence being a portion of the base sequence to be examined;

an evaluation step of calculating specificity of the extracted partial base sequence among the plurality of target sequences, evaluating suitability as a probe of the extracted base sequence based on the calculated specificity and obtaining an evaluation result thereof;

a determination step of determining a partial base sequence as a probe candidate that is utilized for designing a base sequence to be used as a probe which is hybridized with a nucleic acid fragment to perform analysis on the basis of the evaluation result in the evaluation step; and

an output step of outputting the probe candidate to an external storage apparatus, a display apparatus or a printer;

wherein the evaluation step comprises:

calculating the entropy of each node present on the path as the specificity on the basis of the number of times of appearance of a partial base sequence corresponding to the node in the target base sequences;

introducing an evaluation function which multiplies a change in the entropy between nodes by a weight which reduces ~~as a~~ in response to the increase of distance ~~from~~ between the center of a partial base sequence ~~to~~ and a node ~~increases~~; and

obtaining an evaluation result based on calculation result of the evaluation function.

**Claim 2** (Original): The method according to claim 1, wherein the plurality of partial base sequences in the generation step are partial base sequences obtained from a complementary base sequence of the target base sequence.

**Claim 3** (Original): The method according to claim 1, wherein

the plurality of partial base sequences in the generation step are partial base sequences obtained from the target base sequence, and

the determination step comprises selecting a partial base sequence on the basis of the evaluation result in the evaluation step, and determining a complementary base sequence of the selected partial base sequence as a partial base sequence to be used as a probe.

**Claim 4** (Original): The method according to claim 1, wherein the generation step comprises generating a tree for typing all partial base sequences obtained on the basis of the target base sequence.

**Claim 5** (Previously presented): The method according to claim 1, wherein the evaluation step comprises introducing an evaluation function which, when a base sequence whose specificity with respect to the target changes over a predetermined amount exists at the center

of a partial base sequence, gives the partial base sequence an evaluation result to be determined to be used as a probe in the determination step.

**Claims 6-7** (Canceled).

**Claim 8** (Original): The method according to claim 5, wherein the determination step comprises determining, as a probe, a partial base sequence corresponding to a node whose value calculated by the evaluation function in the evaluation step exceeds a predetermined value.

**Claim 9** (Previously presented): The method according to claim 1, wherein the determination step comprises determining, as a probe, a partial base sequence corresponding to a node whose change in the entropy exceeds a predetermined value.

**Claim 10** (Original): The method according to claim 1, further comprising the grouping step of grouping the plurality of partial base sequences in accordance with specificity with respect to the target base sequence,

wherein the determination step comprises determining a partial base sequence to be used as a probe from each group on the basis of the evaluation result in the evaluation step.

**Claim 11** (Original): The method according to claim 1, further comprising:

the grouping step of grouping the plurality of partial base sequences in accordance with specificity with respect to the target base sequence; and

the selecting step of selecting a group having specificity appropriate as a probe from groups obtained in the grouping step,

wherein the determination step comprises determining a partial base sequence to be used as a probe, from each group selected in the selecting step, on the basis of the evaluation result in the evaluation step.

**Claim 12** (Canceled).

**Claim 13** (Original): The method according to claim 11, wherein the selecting step comprises eliminating at least a group having no specificity with respect to all targets to be analyzed.

**Claim 14** (Original): The method according to claim 11, wherein the evaluation step comprises evaluating partial base sequences in a group selected in the selecting step.

**Claim 15** (Previously Presented): The method according to claim 10, wherein  
the target contains a plurality of base sequence patterns, and  
the grouping step comprises assigning, to the same group, partial base sequences  
which react to the same base sequence patterns.

**Claim 16** (Previously Presented): The method according to claim 1, wherein in the tree, the  
base sequence order of partial base sequences represented by node connections is identified  
with the base sequence order in the target.

**Claim 17** (Original): The method according to claim 1, wherein in the tree, the base sequence  
order of partial base sequences represented by node connections is changed such that the  
central one of corresponding partial base sequences in the target is the first one.

**Claim 18** (Original): The method according to claim 1, wherein the evaluation step  
comprises evaluating only a partial base sequence having a length within a previously  
designated range.

**Claim 19** (Original): The method according to claim 1, wherein the evaluation step  
comprises evaluating only a partial base sequence meeting a melting temperature condition  
within a previously designated range.

**Claim 20** (Original): The method according to claim 1, wherein the determination step  
comprises determining a partial base sequence as a probe, from partial base sequences having

lengths within a previously designated range, on the basis of the evaluation result in the evaluation step.

**Claim 21** (Original): The method according to claim 1, wherein the determination step comprises determining a partial base sequence as a probe, from partial base sequences meeting a melting temperature condition within a previously designated range, on the basis of the evaluation result in the evaluation step.

**Claim 22** (Withdrawn): A probe designing method of designing a base sequence to be used as a probe which is hybridized with an unknown nucleic acid fragment to perform gene analysis, comprising:

the generation step of generating a partial base sequence hash table for typing partial base sequences obtained on the basis of a target base sequence and having a specific length;

the evaluation step of evaluating the suitability as a probe of a partial base sequence present in the base sequence hash table, on the basis of the base sequence thereof; and

the determination step of determining a partial base sequence to be used as a probe on the basis of the evaluation result in the evaluation step.

**Claim 23** (Withdrawn): The method according to claim 22, wherein the partial base sequences in the generation step are partial base sequences obtained from a complementary base sequence of the target base sequence.

**Claim 24** (Withdrawn): The method according to claim 22, wherein

the partial base sequences in the generation step are partial base sequences obtained from the target base sequence, and

the determination step comprises selecting a partial base sequence on the basis of the evaluation result in the evaluation step, and determining a complementary base sequence of the selected partial base sequence as a partial base sequence to be used as a probe.

**Claim 25** (Withdrawn): The method according to claim 22, wherein the generation step comprises generating a plurality of hash tables in accordance with partial base sequences having different lengths.

**Claim 26** (Withdrawn): The method according to claim 22, wherein the evaluation step comprises introducing an evaluation function which, when a base sequence whose specificity with respect to the target changes exists near the center of a partial base sequence, evaluates that the partial base sequence is adequate as a probe.

**Claim 27** (Withdrawn): The method according to claim 22, wherein

a plurality of targets exist, and

the evaluation step comprises obtaining a specific position at which base sequences are different between a plurality of base sequences of the plurality of targets, and evaluating the suitability as a probe on the basis of the specific position in a partial base sequence registered in the hash table.

**Claim 28** (Withdrawn): The method according to claim 27, wherein the evaluation step comprises checking whether the specific position is in the center of a base sequence, in order to evaluate the suitability as a probe.

**Claim 29** (Withdrawn): The method according to claim 26, wherein the determination step comprises selecting a probe whose value calculated by the evaluation function in the evaluation step exceeds a predetermined value.

**Claim 30** (Withdrawn): The method according to claim 22, further comprising the grouping step of grouping the plurality of partial base sequences in accordance with the specificity with respect to the target,

wherein the determination step comprises determining a partial base sequence to be used as a probe from each group on the basis of the evaluation result in the evaluation step.

**Claim 31** (Withdrawn): The method according to claim 22, further comprising:

the grouping step of grouping the plurality of partial base sequences in accordance with specificity with respect to the target; and

the selecting step of selecting a group having specificity appropriate as a probe from groups obtained in the grouping step,

wherein the determination step comprises determining a partial base sequence to be used as a probe, from each group selected in the selecting step, on the basis of the evaluation result in the evaluation step.

**Claim 32** (Withdrawn): The method according to claim 31, wherein the selecting step comprises selecting only a necessary and sufficient group completely independent in terms of information.

**Claim 33** (Withdrawn): The method according to claim 31, wherein the selecting step comprises eliminating at least a group having no specificity with respect to a plurality of targets to be analyzed.

**Claim 34** (Withdrawn): The method according to claim 31, wherein the evaluation step comprises evaluating partial base sequences in a group selected in the selecting step.

**Claim 35** (Withdrawn): The method according to claim 30, wherein

the target contains a plurality of base sequence patterns, and

the grouping step comprises assigning, to the same group, partial base sequences which react or do not react identically with each of the plurality of base sequence patterns.

**Claim 36** (Withdrawn): The method according to claim 22, wherein the evaluation step comprises evaluating only a partial base sequence meeting a melting temperature condition within a previously designated range.

**Claim 37** (Withdrawn): The method according to claim 22, wherein the determination step comprises determining a partial base sequence as a probe, from partial base sequences meeting a melting temperature condition within a previously designated range, on the basis of the evaluation result in the evaluation step.

**Claim 38** (Withdrawn): A probe designing method of designing a base sequence to be used as a probe which is hybridized with an unknown nucleic acid fragment to perform gene analysis, comprising:

the generation step of generating a discrimination tree for typing a list of a plurality of partial base sequences obtained from target base sequence data;

the evaluation step of evaluating the suitability as a probe of a probe candidate present in the discrimination tree; and

the selecting step of selecting a probe to be used on the basis of the evaluation result in the evaluation step.

**Claim 39** (Withdrawn): The method according to claim 38, wherein the target base sequence data contains all base sequences which can exist in a specimen.

**Claim 40** (Withdrawn): The method according to claim 38, wherein the target base sequence data contains all base sequences which can exist in a specimen and a specific base sequence.



**Claim 41** (Withdrawn): The method according to claim 40, wherein the evaluation step comprises evaluating a probe candidate formed by a partial sequence of the specific base sequence.

**Claim 42** (Withdrawn): A probe designing method of designing a base sequence to be used as a probe which is hybridized with an unknown nucleic acid fragment to perform gene analysis, comprising:

the generation step of generating a partial base sequence hash table for typing a list of a plurality of partial base sequences obtained from target base sequence data and having a specific length;

the evaluation step of evaluating the suitability as a probe of a probe candidate present in the partial base sequence hash table; and

the selecting step of selecting a probe to be used on the basis of the evaluation result in the evaluation step.

**Claim 43** (Withdrawn): The method according to claim 42, wherein the target base sequence data contains all base sequences which can exist in a specimen.

**Claim 44** (Withdrawn): The method according to claim 42, wherein the target base sequence data contains all base sequences which can exist in a specimen and a specific base sequence.

**Claim 45** (Withdrawn): The method according to claim 44, wherein the evaluation step comprises evaluating a probe candidate formed by a partial sequence of the specific base sequence.

**Claim 46** (Currently amended): An information processing apparatus for performing the method of determining a probe candidate that is utilized for designing a base sequence to be

used as a probe which is hybridized with a nucleic acid fragment to perform analysis, said apparatus comprising:

generation means for generating a tree in which a plurality of partial base sequences obtained on the basis of a plurality of target base sequences are arranged on nodes, said target base sequences including a base sequence to be examined;

extraction means for extracting a partial base sequence indicated by nodes present on a path from one of the nodes to a root node on the tree, the partial base sequence being a portion of the base sequence to be examined;

evaluation means for calculating specificity of the extracted partial base sequence among the plurality of target sequences, evaluating suitability as a probe of the extracted base sequence based on the calculated specificity and obtaining an evaluation result thereof;

determination means for determining a partial base sequence as a probe candidate that is utilized for designing a base sequence to be used as a probe which is hybridized with a nucleic acid fragment to perform analysis on the basis of the evaluation result in said evaluation means; and

output means for outputting the probe candidate to an external storage apparatus, a display apparatus or a printer;

wherein said evaluation means calculates the entropy of each node present on the path as the specificity on the basis of the number of times of appearance of a partial base sequence corresponding to the node in the target base sequences, introduces an evaluation function which multiplies a change in the entropy between nodes by a weight which reduces as a in response to the increase of distance from between the center of a partial base sequence to and

a node ~~increases~~, and obtains an evaluation result based on calculation result of the evaluation function.

**Claim 47** (Cancelled).

**Claim 48** (Previously presented): A storage medium storing a program adapted to control a computer to perform the method of determining a probe candidate according to claim 1.

**Claim 49** (Withdrawn): A DNA microarray comprising a base probe determined by using the probe designing method according to claim 1.

**Claim 50** (Withdrawn): A gene inspecting apparatus comprising a base probe determined by using the probe designing method according to claim 1.

**Claim 51** (Previously Presented): A method of designing a probe including the steps of determining and outputting a probe candidate in accordance with claim 1, and using the probe candidate to design a probe.